WHAT IS CLAIMED IS:

1. An NO-donating compound or a pharmaceutically acceptable salt thereof, comprising an NO-releasing group and a chemical moiety being covalently attached to said NO-releasing group, such that when NO is released from the compound a residue which is a naturally occurring metabolite is formed, thereby preventing or decreasing a development of tolerance to the NO-donating compound upon repetitive administration thereof,

with the proviso that the NO-donating compound is not 1-(4-methylthiazol-5-yl)ethane-1,2-diyl dinitrate and 2-(4-methylthiazol-5-yl)ethyl nitrate.

2. The NO-donating compound of claim 1, wherein said NO-releasing group is selected from the group consisting of a $-ONO_2$ group, a –SNO group, a diazeniumdiolate and a mesoionic oxatriazole.

3. The NO-donating compound of claim 1, further comprising a bioactive agent residue covalently attached to said chemical moiety.

4. The NO-donating compound of claim 3, wherein said bioactive agent residue is attached to said chemical moiety via a biocleavable moiety.

5. The NO-donating compound of claim 3, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid

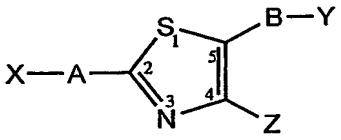
residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

6. The NO-donating compound of claim 4, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

7. The NO-donating compound of claim 1, wherein said naturally occurring metabolite is a thiamine metabolite.

8. The NO-donating compound of claim 7, wherein said chemical moiety comprises a substituted or unsubstituted thiazole ring.

9. The NO-donating compound of claim 8, having the general formula I:



Formula I

wherein:

A is selected from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cycloalkyl, diazo, disulfide, guanidine, guanyl, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, oxygen, sulfur, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, sulfur, thioalkoxy, thioaryloxy, thiocarbonyl,

thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a biocleavable moiety and any combination thereof, or absent;

X is selected from the group consisting of acyl-halide, alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cyano, cycloalkyl, diazo, disulfide, guanidine, guanyl, halide, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, hydrogen, hydroxy, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, thioalkoxy, thioaryloxy, thiocarbonyl, thiohydroxy, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a bioactive agent residue, a moiety containing at least one NO-releasing group, a substituted or unsubstituted thiazole and any combination thereof;

B is selected from the group consisting of a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms, and a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms interrupted by at least one heteroatom, whereby said at least one heteroatom comprises oxygen, sulfur, nitrogen, phosphor, silicon and any combination thereof;

Y is said NO-releasing group; and

Z is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, amine, cycloalkyl, heteroalicyclic, aryl, heteroaryl, halide, haloalkyl, hydroxy, thiohydroxy, alkoxy, thioalkoxy, aryloxy and thioaryloxy.

10. The NO-donating compound of claim 9, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue,

an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

11. The NO-donating compound of claim 10, wherein said bioactive agent residue is a non-steroidal anti-inflammatory drug residue.

12. The NO-donating compound of claim 11, wherein said non-steroidal anti-inflammatory drug is selected from the group consisting of aspirin, celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, oxyphenbutazone, phenylbutazone, piroxicam, rofecoxib sulindac and tolmetin.

13. The NO-donating compound of claim 10, wherein said bioactive agent residue is an anti-diabetic agent residue.

14. The NO-donating compound of claim 13, wherein said anti-diabetic agent is selected from the group consisting of acarbose, acetohexamide, chlorpropamide, glimepiride, glipizide, glyburide, lipoic acid, meglitol, metformin, miglitol, nateglinide, pioglitazone, repaglinide, rosiglitazone, tolazamide, tolbutamide and troglitazone.

15. The NO-donating compound of claim 9, wherein said NO-releasing group in said Y is selected from the group consisting of a $-ONO_2$ group, a –SNO group, a diazeniumdiolate and a mesoionic oxatriazole.

16. The NO-donating compound of claim 15, wherein said NO-releasing group in said Y is a $-ONO_2$ group.

17. The NO-donating compound of claim 16, wherein Z is alkyl.

18. The NO-donating compound of claim 17, wherein said alkyl is methyl.

19. The NO-donating compound of claim 18, wherein B is an ethylene chain.

20. The NO-donating compound of claim 9, wherein B is selected from the group consisting of $-CH_2-CH_2-O-CH_2-$, $-CH_2-CH_2-NH-CH_2-$ and $-CH_2-CH_2-S-CH_2-$.

21. The NO-donating compound of claim 20, wherein Z is alkyl.

22. The NO-donating compound of claim 21, wherein said alkyl is methyl.

23. The NO-donating compound of claim 21, wherein said NO-releasing group in said Y is $-ONO_2$.

24. The NO-donating compound of claim 23, wherein X is hydrogen.

25. The NO-donating compound of claim 23, wherein X is alkyl.

26. The NO-donating compound of claim 25, wherein said alkyl is selected from the group consisting of methyl, ethyl and isopropyl.

27. The NO-donating compound of claim 19, wherein X is alkyl.

28. The NO-donating compound of claim 27, wherein said alkyl is selected from the group consisting of methyl, ethyl and isopropyl.

29. The NO-donating compound of claim 19, wherein X is haloalkyl.

30. The NO-donating compound of claim 29, wherein said haloalkyl is trifluoromethyl.

31. The NO-donating compound of claim 19, wherein X is aryl.

32. The NO-donating compound of claim 31, wherein said aryl is selected from the group consisting of a substituted phenyl and an unsubstituted phenyl.

33. The NO-donating compound of claim 32, wherein said substituted phenyl is selected from the group consisting of 4-trifluoromethylphenyl and pentafluorophenyl.

34. The NO-donating compound of claim 19, wherein X is heteroaryl.

35. The NO-donating compound of claim 34, wherein said heteroaryl is pyridin-3-yl.

36. The NO-donating compound of claim 19, wherein X is heteroalicyclic.

37. The NO-donating compound of claim 36, wherein said heteroalicyclic is piperidine-4-yl.

38. The NO-donating compound of claim 19, wherein X is amine.

39. The NO-donating compound of claim 38, wherein said amine is selected from the group consisting of $-NH_2$ and $-N(CH_3)_2$.

40. The NO-donating compound of claim 19, wherein X is alkoxy.

41. The NO-donating compound of claim 40, wherein said alkoxy is methoxy.

42. The NO-donating compound of claim 19, wherein X is a moiety containing at least one NO-releasing group.

43. The NO-donating compound of claim 42, wherein said moiety is selected from the group consisting of 1-nitrooxy-ethyl, [4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-diazene, 4-methyl-5-(2-nitrooxy-ethyl)-thiazole and 2-butyl-4-methyl-5-(2-nitrooxy-ethyl)-thiazole.

44. The NO-donating compound of claim 19, wherein X is a non-steroidal anti-inflammatory drug residue.

45. The NO-donating compound of claim 44, wherein said non-steroidal anti-inflammatory drug residue is selected from the group consisting of an aspirin residue, an ibuprofen residue and a naproxen residue.

46. The NO-donating compound of claim 19, wherein X is an anti-diabetic agent residue.

47. The NO-donating compound of claim 46, wherein said anti-diabetic agent residue is a lipoic acid residue.

48. The NO-donating compound of claim 9, wherein A is a biocleavable moiety.

49. The NO-donating compound of claim 48, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

50. The NO-donating compound of claim 48, wherein X is a bioactive agent residue.

51. The NO-donating compound of claim 48, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

52. The NO-donating compound of claim 50, wherein said bioactive agent residue is a non-steroidal anti-inflammatory drug residue.

53. The NO-donating compound of claim 52, wherein said non-steroidal anti-inflammatory drug is selected from the group consisting of aspirin, celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, oxyphenbutazone, phenylbutazone, piroxicam, rofecoxib sulindac and tolmetin.

54. The NO-donating compound of claim 50, wherein said bioactive agent residue is an anti-diabetic agent residue.

55. The NO-donating compound of claim 54, wherein said anti-diabetic drug is selected from the group consisting of acarbose, acetohexamide,

chlorpropamide, glimepiride, glipizide, glyburide, lipoic acid, meglitol, metformin, miglitol, nateglinide, pioglitazone, repaglinide, rosiglitazone, tolazamide, tolbutamide and troglitazone.

56. The NO-donating compound of claim 1, being selected from the group consisting of the compounds set forth in Table 1 and Table 2.

57. A pharmaceutical composition comprising, as an active ingredient, the NO-donating compound of claim 1 and a pharmaceutically acceptable carrier.

58. A pharmaceutical composition comprising, as an active ingredient, the NO-donating compound of claim 9 and a pharmaceutically acceptable carrier.

59. The pharmaceutical composition of claim 57, being packaged in a packaging material and identified in print, in or on said packaging material, for use in the treatment of a medical condition in which modulating an NO level is beneficial.

60. The pharmaceutical composition of claim 59, wherein said modulating comprises elevating said NO level.

61. The pharmaceutical composition of claim 59, wherein said medical condition is selected from the group consisting of a cardiovascular disease or disorder, a gastrointestinal disease or disorder, an inflammatory disease or disorder, a respiratory disease or disorder, a central nervous system disease or disorder, a neurodegenerative disease or disorder, a psychiatric disease or disorder, a blood pressure-associated disease or disorder, a coronary artery disease or disorder, atherosclerosis, a cholesterol level-associated disease or disorder, an arterial thrombotic disease or disorder, a heart failure, a stroke, a septic shock, a NSAID-induced gastric disease or disorder, an inflammatory bowel disease or disorder, an ischemic renal disease or disorder, a peptic ulcer, diabetes, pulmonary hypertension, sickle cell anemia, asthma, a chronic obstructive pulmonary disease or disorder, dementia, epilepsy, a neuroinflammatory disease or disorder, trauma, multiple

sclerosis, an erectile dysfunction, a male and female sexual dysfunction and an age-related disease or disorder.

62. A method of treating or preventing a medical condition in which modulating an NO level is beneficial, the method comprising administering to a subject in need thereof a therapeutically effective amount of the NO-donating compound of claim 1.

63. The method of claim 62, wherein said modulating comprises elevating said NO level.

64. The method of claim 62, wherein said medical condition is selected from the group consisting of a cardiovascular disease or disorder, a gastrointestinal disease or disorder, an inflammatory disease or disorder, a respiratory disease or disorder, a central nervous system disease or disorder, a neurodegenerative disease or disorder, a psychiatric disease or disorder, a blood pressure-associated disease or disorder, a coronary artery disease or disorder, atherosclerosis, a cholesterol level-associated disease or disorder, an arterial thrombotic disease or disorder, a heart failure, a stroke, a septic shock, a NSAID-induced gastric disease or disorder, an inflammatory bowel disease or disorder, an ischemic renal disease or disorder, a peptic ulcer, diabetes, pulmonary hypertension, sickle cell anemia, asthma, a chronic obstructive pulmonary disease or disorder, dementia, epilepsy, a neuroinflammatory disease or disorder, trauma, multiple sclerosis, an erectile dysfunction, a male and female sexual dysfunction and an age-related disease or disorder.

65. The method of claim 62, wherein said administering is effected orally, rectally, intravenously, topically, intranasally, intradermally, transdermally, subcutaneously, intramuscularly, intrperitoneally, intraperitoneally, by inhalation or by intrathecal catheter.

66. The method of claim 62, further comprising administering to said subject an additional active ingredient, said additional active ingredient being capable of treating or preventing the medical condition.

67. The method of claim 62, wherein said compound is administered either per se or as a part of a pharmaceutical composition, said pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

68. A method of treating or preventing a medical condition in which modulating an NO level is beneficial, the method comprising administering to a subject in need thereof a therapeutically effective amount of the NO-donating compound of claim 9.

69. The method of claim 68, wherein said modulating comprises elevating said NO level.

70. The method of claim 68, wherein the medical condition is selected from the group consisting of a cardiovascular disease or disorder, a gastrointestinal disease or disorder, an inflammatory disease or disorder, a respiratory disease or disorder, a central nervous system disease or disorder, a neurodegenerative disease or disorder, a psychiatric disease or disorder, a blood pressure-associated disease or disorder, a coronary artery disease or disorder, atherosclerosis, a cholesterol level-associated disease or disorder, an arterial thrombotic disease or disorder, a heart failure, a stroke, a septic shock, a NSAID-induced gastric disease or disorder, an inflammatory bowel disease or disorder, an ischemic renal disease or disorder, a peptic ulcer, diabetes, pulmonary hypertension, sickle cell anemia, asthma, a chronic obstructive pulmonary disease or disorder, dementia, epilepsy, a neuroinflammatory disease or disorder, trauma, multiple sclerosis, an erectile dysfunction, a male and female sexual dysfunction and an age-related disease or disorder.

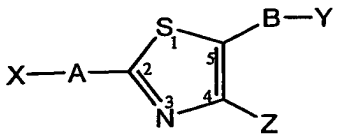
71. The method of claim 68, wherein said administering is effected orally, rectally, intravenously, topically, intranasally, intradermally, transdermally, subcutaneously, intramuscularly, intrperitoneally, intraperitoneally, by inhalation or by intrathecal catheter.

72. The method of claim 68, wherein said therapeutically effective amount ranges between about 0.01 mg/kg body and about 5 mg/kg body.

73. The method of claim 68, further comprising administering to said subject an additional active ingredient, said additional active ingredient being capable of treating or preventing the medical condition.

74. The method of claim 68, wherein said compound is administered either per se or as a part of a pharmaceutical composition, said pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

75. A method of synthesizing a compound having the general formula I:



Formula I

or a pharmaceutically acceptable salt thereof,

wherein:

A is selected from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cycloalkyl, diazo, disulfide, guanidine, guanyl, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, oxygen, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, sulfur, thioalkoxy, thioaryloxy, thiocarbonyl, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea and any combination thereof, or absent;

X is selected from the group consisting of acyl-halide, alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cyano, cycloalkyl, diazo, disulfide, guanidine, guanyl, halide, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, hydrogen, hydroxy, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate,

O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, thioalkoxy, thioaryloxy, thiocarbonyl, thiohydroxy, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a bioactive agent residue, a moiety containing at least one NO-releasing group, a substituted or unsubstituted thiazole and any combination thereof;

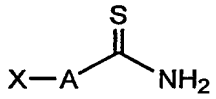
B is selected from the group consisting of a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms, and a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms interrupted by at least one heteroatom, whereby said at least one heteroatom comprises oxygen, sulfur, nitrogen, phosphor, silicon and any combination thereof;

Y is an NO-releasing group; and

Z is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, amine, cycloalkyl, heteroalicyclic, aryl, heteroaryl, halide, haloalkyl, hydroxy, thiohydroxy, alkoxy, thioalkoxy, aryloxy and thioaryloxy;

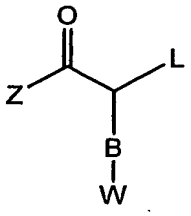
the method comprising:

providing a thioamide having a general formula II:



Formula II

providing a reactive compound having the general formula III:



Formula III

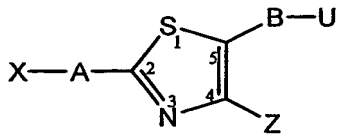
wherein:

L is a leaving group;

Z and B are as defined above; and

W is a pre-nitratable group;

reacting said thioamide having said general formula II and said compound having said general formula III, to thereby generate a thiazole derivative having a general formula IV:



Formula IV

wherein:

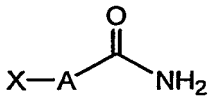
A, X, B and Z are as defined above; and

U is a nitratable group; and

converting said nitratable group into an NO-releasing group, thereby obtaining the compound having the general formula I.

76. The method of claim 75, wherein providing said thioamide comprises:

providing an amide having a general formula V:



Formula V

wherein:

X and A are as defined above; and

reacting said amide with a thiolating agent.

77. The method of claim 76, wherein said thiolating agent is phosphorous pentasulfide.

78. The method of claim 75, wherein said pre-nitratable group is selected from the group consisting of alkoxy, aryloxy, thioalkoxy, thioaryloxy, silanoxy, silicate and O-carboxylate.

79. The method of claim 75, wherein said nitratable group is selected from the group consisting of hydroxy and thiohydroxy.

80. The method of claim 75, wherein said converting comprises reacting said thiazole derivative having said formula IV with a nitrating agent, said nitrating agent containing said NO-releasing moiety.

81. The method of claim 80, wherein said NO-releasing moiety is ONO_2 and said nitrating agent is nitric acid.

82. The method of claim 79, wherein said NO-releasing moiety is ONO_2 and said nitrating agent is nitric acid.

83. The method of claim 75, wherein said leaving group is selected from the group consisting of halide, alkoxy, aryloxy, amine, hydroxy, azide, nitro, cyano, thiocyanate, O-carboxylate, thiohydroxy and sulfonate.

84. The method of claim 75, wherein said leaving group is a halide.

85. The method of claim 75, wherein Z is alkyl.

86. The method of claim 85, wherein said alkyl is methyl.

87. The method of claim 75, wherein B is an ethylene chain.

88. The method of claim 75, wherein said pre-nitratable group is acetate and said nitratable group is hydroxy.

89. The method of claim 75, wherein said reactive compound having said general formula III is 5-acetoxy-3-chloro-2-pentanone.

90. The method of claim 75, wherein B is selected from the group consisting of $-CH_2-CH_2-O-CH_2-$, $-CH_2-CH_2-NH-CH_2-$ and $-CH_2-CH_2-S-CH_2-$.

91. The method of claim 90, wherein Z is alkyl.

92. The method of claim 91, wherein said alkyl is methyl.

93. The method of claim 90, wherein X is hydrogen.

94. The method of claim 90, wherein X is alkyl.

95. The method of claim 94, wherein said alkyl is selected from the group consisting of methyl, ethyl and isopropyl.

96. The method of claim 75, wherein A is a biocleavable moiety.

97. The method of claim 96, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

98. The method of claim 75, wherein X is a bioactive agent residue.

99. The method of claim 98, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal

anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

100. The method of claim 98, wherein said bioactive agent residue is a non-steroidal anti-inflammatory drug residue.

101. The method of claim 100, wherein said non-steroidal anti-inflammatory drug is selected from the group consisting of aspirin, celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, oxyphenbutazone, phenylbutazone, piroxicam, rofecoxib sulindac and tolmetin.

102. The method of claim 98, wherein said bioactive agent residue is an anti-diabetic agent residue.

103. The method of claim 102, wherein said anti-diabetic agent is selected from the group consisting of acarbose, acetohexamide, chlorpropamide, glimepiride, glipizide, glyburide, lipoic acid, meglitol, metformin, miglitol, nateglinide, pioglitazone, repaglinide, rosiglitazone, tolazamide, tolbutamide and troglitazone.

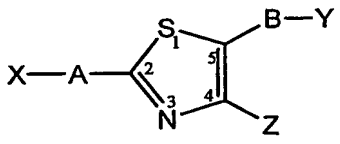
104. The method of claim 75, wherein said thioamide having said general formula II is selected from the group consisting of N,N-dimethylthiourea,

thiobenzamide, thiourea, N-allylthiourea, acetylthiourea, N-ethylthiourea, N,N-dimethylthiourea, alpha-naphthylthiourea, 1-[(3,5-bis-trifluoromethyl)phenyl]thiourea and dithiooxalamide.

105. The method of claim 76, wherein said amide is selected from the group consisting of propionamide, acetamide, isobutyramide, L-(-)-lactamide, trifluoroacetamide, carbamic acid methyl ester, hexanedioic acid diamide, piperidine-4-carboxylic acid amide, thionicotinamide, naproxenamide, 4-(trifluoromethyl)-thiobenzamide, azodicarbonamide, 2-(4-isobutyl-phenyl)-propionamide, isonicotinamide, 2,2,2-trifluoroacetamide, glycinamide, 4-aminobenzamide, 2,3,4,5,6-pentafluorobenzamide, 2-aminobenzamide, ethyloxamate, 2,6-difluorobenzamide, N-phenylurea, 2,4-dichlorophenylacetamide, 2,4-dichlorophenoxyacetmide, 2-phenylbutyamide, azodicarbonamide, 3,5-difluorobenzamide, DL-lipoamide, Rubeanic acid, adpamide, aalonamide, acrylamide and 2-hydroxy-benzamide.

106. The method of claim 75, wherein said compound is selected from the group of compounds set forth in Table 1 and Table 2.

107. A method of synthesizing a compound having the general formula I:



Formula I

or a pharmaceutically acceptable salt thereof,

wherein:

A is a biocleavable moiety;

X is selected from the group consisting of acyl-halide, alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cyano, cycloalkyl, diazo, disulfide, guanidine,

guanyl, halide, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, hydrogen, hydroxy, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, thioalkoxy, thioaryloxy, thiocarbonyl, thiohydroxy, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a bioactive agent residue, a moiety containing at least one NO-releasing group, a substituted or unsubstituted thiazole and any combination thereof;

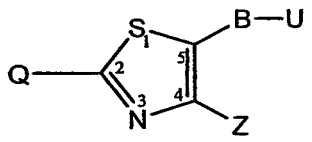
B is selected from the group consisting of a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms, and a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms interrupted by at least one heteroatom, whereby said at least one heteroatom comprises oxygen, sulfur, nitrogen, phosphor, silicon and any combination thereof;

Y is an NO-releasing group; and

Z is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, amine, cycloalkyl, heteroalicyclic, aryl, heteroaryl, halide, haloalkyl, hydroxy, thiohydroxy, alkoxy, thioalkoxy, aryloxy and thioaryloxy;

the method comprising:

providing a thiazole having a general formula VI:



Formula VI

wherein:

Z, B and U are as defined above; and

Q is a first reactive group;

providing a compound the general formula VII:

X——K

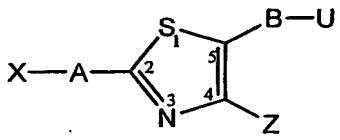
Formula VII

wherein:

X is as defined above; and

K is a second reactive group;

reacting said thiazole having said general Formula VI and said compound having said general Formula VII, to thereby generate a thiazole derivative having a general Formula IV:



Formula IV

wherein:

A, X, B and Z are as defined above; and

U is a nitratable group; and

converting said nitratable group into an NO-releasing group, thereby obtaining the compound having the general Formula I.

108. The method of claim 107, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

109. The method of claim 107, wherein each of said first reactive group and said second reactive group is independently selected from the group consisting of amine, halide, acyl-halide, sulfonate, sulfoxides, phosphate, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, cyano, nitro, azo, isocyanate, sulfonamide, C-carboxylate, O-carboxylate, N-thiocarbamate, O-thiocarbamate, urea, thiourea, O-carbamate, N-carbamate, C-amide, N-amide, guanyl, guanidine and hydrazine.

110. The method of claim 109, wherein each of said first reactive group and said second reactive group is independently selected from the group consisting of amine, hydrazine, alkoxy, halide and carboxylate.

111. The method of claim 107, wherein said nitratable group is selected from the group consisting of hydroxy and thiohydroxy.

112. The method of claim 107, wherein said converting comprises reacting said thiazole derivative having said Formula IV with a nitrating agent, said nitrating agent containing said NO-releasing moiety.

113. The method of claim 112, wherein said NO-releasing moiety is ONO_2 and said nitrating agent is nitric acid.

114. The method of claim 107, wherein Z is alkyl.

115. The method of claim 114, wherein said alkyl is methyl.

116. The method of claim 107, wherein B is an ethylene chain.

117. The method of claim 107, wherein X is a bioactive agent residue.

118. The method of claim 117, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin

inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

119. The method of claim 117, wherein said bioactive agent residue is a non-steroidal anti-inflammatory drug residue.

120. The method of claim 119, wherein said non-steroidal anti-inflammatory drug is selected from the group consisting of aspirin, celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, oxyphenbutazone, phenylbutazone, piroxicam, rofecoxib sulindac and tolmetin.

121. The method of claim 117, wherein said bioactive agent residue is an anti-diabetic agent residue.

122. The method of claim 121, wherein said anti-diabetic agent is selected from the group consisting of acarbose, acetohexamide, chlorpropamide, glimepiride, glipizide, glyburide, lipoic acid, meglitol, metformin, miglitol, nateglinide, pioglitazone, repaglinide, rosiglitazone, tolazamide, tolbutamide and troglitazone.

123. The method of claim 107, wherein said thiazole having a general formula VI is selected from the group consisting of 2-(2-amino-4-methyl-thiazol-5-yl)-ethanol and 5-(2-hydroxy-ethyl)-4-methyl-thiazole-2-carboxylic.

124. The method of claim 107, wherein said compound having the general formula VII is selected from consisting of 2-(6-methoxy-naphthalen-2-yl)-propionic acid, 4-[1,2]dithiolan-3-yl-butyric acid, 2-(4-isobutyl-phenyl)-propionic acid, nicotinic acid, 1-oxy-nicotinic acid, 2,6-difluoro-benzoic acid, phthalazin-1-yl-

hydrazine, 3-chloro-propene, 4-acetylamino-benzoic acid, hexadecanoic acid, 2-acetoxy-benzoic acid, pyrrolidine-2-carboxylic acid, (2,4-dichloro-phenyl)-acetic acid, (2,4-dichloro-phenoxy)-acetic acid and 17-hydroxy-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-cyclopenta[a]phenanthren-3-one.

125. A medical device comprising the NO-donating compound of claim 1 and a delivery system configured for delivering said NO-donating compound to a bodily site of a subject.

126. The medical device of claim 125, wherein said NO-donating compound forms a part of a pharmaceutical composition, said pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

127. The medical device of claim 125, wherein said delivering is effected by inhalation.

128. The medical device of claim 127, wherein said delivery system is selected from the group consisting of a metered dose inhaler, a respirator, a nebulizer inhaler, a dry powder inhaler, an electric warmer, a vaporizer, an atomizer and an aerosol generator.

129. The medical device of claim 125, wherein said delivering is effected transdermally.

130. The medical device of claim 129, wherein said delivery system is selected from the group consisting of an adhesive plaster and a skin patch.

131. The medical device of claim 125, wherein said delivering is effected topically.

132. The medical device of claim 131, wherein said delivery system is selected from the group consisting of an adhesive strip, a bandage, an adhesive plaster, a wound dressing and a skin patch.

133. The medical device of claim 125, wherein said delivering is effected by implanting the medical device in a bodily organ.

134. The medical device of claim 133, wherein said delivery system comprises a biocompatible matrix.

135. The medical device of claim 134, wherein said biocompatible matrix comprises a biodegradable polymer.

136. The medical device of claim 135, wherein said biocompatible matrix comprises a slow release carrier.

137. The medical device of claim 133, wherein said delivery system is selected from the group consisting of an aortic aneurysm graft device, an atrioventricular shunt, a catheter, a defibrilator, a heart valve, a hemodialysis catheter, a hemodialysis graft, an indwelling arterial catheter, an indwelling venous catheter, a needle, a pacemaker, a pacemaker lead, a patent foramen ovale septal closure device, a stent, a stent graft, a suture, a synthetic vascular graft, a thread, a tube, a vascular anastomosis clip, a vascular aneurysm occluder, a vascular clip, a vascular prosthetic filter, a vascular sheath and a drug delivery port, a venous valve and a wire.

138. The medical device of claim 133, wherein said organ is selected from the group consisting of a pulmonary cavity, a blood vessel, an artery, a vein, a capillary, a heart, a heart cavity and a visceral organ.

139. The medical device of claim 125, wherein said bodily site in selected from the group consisting of skin, scalp, a dermal layer, an eye, an ear, a small intestines tissue, a large intestines tissue, a kidney, a pancreas, a liver, a digestive tract, a respiratory tract, a bone, a bone marrow tissue, a mucosal membrane, a nasal membrane, the blood system, a blood vessel, a muscle, a pulmonary cavity, an artery, a vein, a capillary, a heart, a heart cavity, a male reproductive organ, a female reproductive organ and a visceral organ.

140. Use of an NO-donating compound or a pharmaceutically acceptable salt thereof comprising an NO-releasing group and a chemical moiety being covalently attached to said NO-releasing group and being designed such that when NO is released from the compound a residue which is a naturally occurring metabolite is formed, thereby preventing or decreasing a development of tolerance to the NO-donating compound upon repetitive administration thereof, in the treatment of a medical condition in which modulating an NO level is beneficial, with the proviso that the NO-donating compound is not 1-(4-methylthiazol-5-yl)ethane-1,2-diyl dinitrate and 2-(4-methylthiazol-5-yl)ethyl nitrate.

141. Use of an NO-donating compound comprising an NO-releasing group and a chemical moiety being covalently attached to said NO-releasing group and being designed such that when NO is released from the compound a residue which is a naturally occurring metabolite is formed, thereby preventing or decreasing a development of tolerance to the NO-donating compound upon repetitive administration thereof, for the preparation of a medicament for treating a medical condition in which modulating an NO level is beneficial, with the proviso that the NO-donating compound is not 1-(4-methylthiazol-5-yl)ethane-1,2-diyl dinitrate and 2-(4-methylthiazol-5-yl)ethyl nitrate.

142. The use of any of claims 140 and 141, wherein said modulating comprises elevating said NO level.

143. The use of any of claims 140 and 141, wherein the medical condition is selected from the group consisting of a cardiovascular disease or disorder, a gastrointestinal disease or disorder, an inflammatory disease or disorder, a respiratory disease or disorder, a central nervous system disease or disorder, a neurodegenerative disease or disorder, a psychiatric disease or disorder, a blood pressure-associated disease or disorder, a coronary artery disease or disorder, atherosclerosis, a cholesterol level-associated disease or disorder, an arterial thrombotic disease or disorder, a heart failure, a stroke, a septic shock, a NSAID-induced gastric disease or disorder, an inflammatory bowel disease or disorder, an ischemic renal disease or disorder, a peptic ulcer, diabetes, pulmonary hypertension, sickle cell anemia, asthma, a chronic

obstructive pulmonary disease or disorder, dementia, epilepsy, a neuroinflammatory disease or disorder, trauma, multiple sclerosis, an erectile dysfunction, a male and female sexual dysfunction and an age-related disease or disorder.

144. The use of any of claims 140 and 141, wherein said NO-releasing group is selected from the group consisting of a $-ONO_2$ group, a –SNO group, a diazeniumdiolate and a mesoionic oxatriazole.

145. The use of any of claims 140 and 141, wherein said NO-donating compound further comprises a bioactive agent residue covalently attached to said chemical moiety.

146. The use of claim 145, wherein said bioactive agent residue is attached to said chemical moiety via a biocleavable moiety.

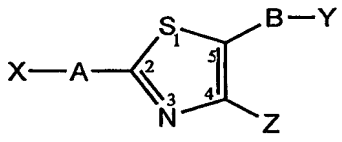
147. The use of claim 145, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

148. The use of claim 146, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

149. The use of any of claims 140 and 141, wherein said naturally occurring metabolite is a thiamine metabolite.

150. The use of claim 149, wherein said chemical moiety comprises a substituted or unsubstituted thiazole ring.

151. The use of claim 150, wherein said NO-donating compound has the general formula I:



Formula I

wherein:

A is selected from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cycloalkyl, diazo, disulfide, guanidine, guanyl, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, oxygen, sulfur, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, sulfur, thioalkoxy, thioaryloxy, thiocarbonyl, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a biocleavable moiety and any combination thereof, or absent;

X is selected from the group consisting of acyl-halide, alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cyano, cycloalkyl, diazo, disulfide, guanidine, guanyl, halide, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, hydrogen, hydroxy,

N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, thioalkoxy, thioaryloxy, thiocarbonyl, thiohydroxy, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a bioactive agent residue, a moiety containing at least one NO-releasing group, a substituted or unsubstituted thiazole and any combination thereof;

B is selected from the group consisting of a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms, and a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms interrupted by at least one heteroatom, whereby said at least one heteroatom comprises oxygen, sulfur, nitrogen, phosphor, silicon and any combination thereof;

Y is said NO-releasing group; and

Z is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, amine, cycloalkyl, heteroalicyclic, aryl, heteroaryl, halide, haloalkyl, hydroxy, thiohydroxy, alkoxy, thioalkoxy, aryloxy and thioaryloxy.

152. The use of claim 151, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid

residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

153. The use of claim 152, wherein said bioactive agent residue is a non-steroidal anti-inflammatory drug residue.

154. The use of claim 153, wherein said non-steroidal anti-inflammatory drug is selected from the group consisting of aspirin, celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, oxyphenbutazone, phenylbutazone, piroxicam, rofecoxib sulindac and tolmetin.

155. The use of claim 152, wherein said bioactive agent residue is an anti-diabetic agent residue.

156. The use of claim 155, wherein said anti-diabetic agent is selected from the group consisting of acarbose, acetohexamide, chlorpropamide, glimepiride, glipizide, glyburide, lipoic acid, meglitol, metformin, miglitol, nateglinide, pioglitazone, repaglinide, rosiglitazone, tolazamide, tolbutamide and troglitazone.

157. The use of claim 151, wherein said NO-releasing group in said Y is selected from the group consisting of a $-ONO_2$ group, a –SNO group, a diazeniumdiolate and a mesoionic oxatriazole.

158. The use of claim 157, wherein said NO-releasing group in said Y is a $-ONO_2$ group.

159. The use of claim 158, wherein Z is alkyl.

160. The use of claim 159, wherein said alkyl is methyl.

161. The use of claim 160, wherein B is an ethylene chain.

162. The use of claim 151, wherein B is selected from the group consisting of $-CH_2-CH_2-O-CH_2-$, $-CH_2-CH_2-NH-CH_2-$ and $-CH_2-CH_2-S-CH_2-$.

163. The use of claim 162, wherein Z is alkyl.

164. The use of claim 163, wherein said alkyl is methyl.

165. The use of claim 163, wherein said NO-releasing group in said Y is $-ONO_2$.

166. The use of claim 165, wherein X is hydrogen.

167. The use of claim 165, wherein X is alkyl.

168. The use of claim 167, wherein said alkyl is selected from the group consisting of methyl, ethyl and isopropyl.

169. The use of claim 161, wherein X is alkyl.

170. The use of claim 169, wherein said alkyl is selected from the group consisting of methyl, ethyl and isopropyl.

171. The use of claim 161, wherein X is haloalkyl.

172. The use of claim 171, wherein said haloalkyl is trifluoromethyl.

173. The use of claim 161, wherein X is aryl.

174. The use of claim 173, wherein said aryl is selected from the group consisting of a substituted or unsubstituted phenyl and a substituted or unsubstituted naphthalenyl.

175. The use of claim 174, wherein said substituted phenyl is selected from the group consisting of 4-trifluoromethylphenyl and pentafluorophenyl.

176. The use of claim 161, wherein X is heteroaryl.

177. The use of claim 176, wherein said heteroaryl is pyridin-3-yl.

178. The use of claim 161, wherein X is heteroalicyclic.

179. The use of claim 178, wherein said heteroalicyclic is piperidine-4-yl.

180. The use of claim 161, wherein X is amine.

181. The use of claim 180, wherein said amine is selected from the group consisting of $-NH_2$ and $-N(CH_3)_2$.

182. The use of claim 161, wherein X is alkoxy.

183. The use of claim 182, wherein said alkoxy is methoxy.

184. The use of claim 161, wherein X is a moiety containing at least one NO-releasing group.

185. The use of claim 184, wherein said moiety is selected from the group consisting of 1-nitrooxy-ethyl, [4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-diazene, 4-methyl-5-(2-nitrooxy-ethyl)-thiazole and 2-butyl-4-methyl-5-(2-nitrooxy-ethyl)-thiazole.

186. The use of claim 161, wherein X is a non-steroidal anti-inflammatory drug residue.

187. The use of claim 186, wherein said non-steroidal anti-inflammatory drug residue is selected from the group consisting of an aspirin residue, an ibuprofen residue and a naproxen residue.

188. The use of claim 161, wherein X is an anti-diabetic agent residue.

189. The use of claim 188, wherein said anti-diabetic agent residue is a lipoic acid residue.

190. The use of claim 151, wherein A is a biocleavable moiety.

191. The use of claim 190, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

192. The use of claim 190, wherein X is a bioactive agent residue.

193. The use of claim 190, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid

residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

194. The use of claim 192, wherein said bioactive agent residue is a non-steroidal anti-inflammatory drug residue.

195. The use of claim 194, wherein said non-steroidal anti-inflammatory drug is selected from the group consisting of aspirin, celecoxib, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, oxyphenbutazone, phenylbutazone, piroxicam, rofecoxib sulindac and tolmetin.

196. The use of claim 192, wherein said bioactive agent residue is an anti-diabetic agent residue.

197. The use of claim 196, wherein said anti-diabetic drug is selected from the group consisting of acarbose, acetohexamide, chlorpropamide, glimepiride, glipizide, glyburide, lipoic acid, meglitol, metformin, miglitol, nateglinide, pioglitazone, repaglinide, rosiglitazone, tolazamide, tolbutamide and troglitazone.

198. The use of any of claims 140 and 141, wherein said NO-donating compound is selected from the group consisting of the compounds set forth in Table 1 and Table 2.